TABLE 2
General Types of T Wave Abnormalities

Type	Examples
Primary	
Organ (Structural)	Hypertrophy, myocyte destruction, fibrosis
Cell (Metabolic)	Physiological (G protein effects), pharmacologic (antiarrhythmic drugs), and pathological (electrolyte abnormalities, cooling of the heart's surface)
Gene (Molecular)	Posttachycardia syndrome, intermittent bundle branch block, T wave evolution after myocardial infarction
Secondary	Conduction abnormalities (bundle branch block, Wolff-Parkinson-White syndrome), ventricular ectopy

Types of Primary T Wave Abnormalities

Primary T wave abnormalities are generally classified according to their contour or morphology, or in terms of the conditions believed to have caused these changes. This article, which focuses on striking differences in the time courses of the appearance and disappearance of primary T wave abnormalities, proposes a classification based on three fundamentally different causal mechanisms (Table 2). These mechanisms: altered organ structure, altered cell metabolism, and altered gene expression, can be viewed as three paradigms in biological regulation that appeared at different times during evolution.[10,11]

The most transient of the primary T wave abnormalities, whose prompt resolution is not consistent with either structural damage to the heart or molecular replacements involving the ion channels that repolarize the ventricles, can be attributed to rapidly reversible metabolic changes in cellular function. At the opposite extreme are the most long lasting of the primary T wave abnormalities, which are generally irreversible. These can usually be related to structural alterations in the walls of the ventricles and so arise from disorders of the heart's function as an organ. As described below, there appears to be a third cause for primary T wave abnormalities that persist much longer than the transient changes caused by cellular abnormalities, but are not associated with obvious organ damage. This article postulates that the third type of repolarization abnormality, which has been referred to as cardiac "memory,"[1,2] arises from molecular replacements involving the channel proteins of the heart's plasma membrane.

Primary T Wave Abnormalities Caused by Altered Cellular and Organ Function

Cellular T wave abnormalities, which appear and disappear rapidly, are brought about by metabolic changes initiated by a variety of physiological, pharmacologic, and pathological stimuli. Physiological causes include exercise-induced T wave changes and "neurogenic T waves," where autonomic neurotransmitters activate G proteins that interact directly with, or alter the phosphorylation of, cardiac ion channels. Pharmacologic causes include the actions of antiarrhythmic and antidepressant drugs that bind to and interfere with ion channels. Pathological causes reflect changes in the intracellular or extracellular environment, such as intracellular acidosis and altered ionic composition in the extracellular fluid surrounding reversibly injured ischemic cells. Structural T wave abnormalities, which unlike the cellular abnormalities are usually irreversible, arise from changes in the walls of the ventricles such as hypertrophy and fibrosis, destruction of myocardial cells in acute myocarditis, and infiltrative cardiomyopathies like amyloid and fibroelastosis.

Long-Lasting Primary T Wave Abnormalities: Possible Role of Altered Gene Expression

A third mechanism, in addition to the cellular and structural causes described above, can also cause primary T wave abnormalities. This third mechanism could involve abnormal potassium channel structure, or as recently shown for the familial long QT syndrome,[13] abnormalities in proteins that regulate potassium channels. Examples of this third mechanism may account for the remarkably slow appearance, and especially disappearance, of T wave abnormalities associated with at least three well-recognized conditions: posttachycardia T wave abnormalities, persistent anterior precordial T wave inversions after episodes of left bundle branch block or right ventricular pacing, and T wave evolution following transient ischemia without myocardial infarction. The often complete normalization of the T waves in these conditions make it unlikely that these long-lasting repolarization abnormalities arise from structural changes

in the heart. On the other hand, these T wave abnormalities last much longer than known disorders of cellular metabolism, such as those listed in Table 2. For these reasons, the clinical examples described above may arise from alterations in the synthesis and assembly of the potassium channels that control ventricular repolarization. This possibility is supported by evidence that these T wave syndromes are associated with stimuli now recognized to induce a growth response in the cells of the myocardium: depolarization (posttachycardia T wave abnormalities), stretch (left bundle branch block and pacing-induced T wave abnormalities), and ischemic "stress" (T wave evolution after ischemia).

Posttachycardia T Wave Abnormalities

In 1935, Graybiel and White[14] described inverted T waves in "two young men in robust health" whose "only evidence of cardiac disability was furnished by a single paroxysm of ventricular tachycardia lasting less than twenty-four hours." These repolarization abnormalities, which persisted after the restoration of sinus rhythm in both patients (in one of whom the tachycardia terminated spontaneously without treatment), returned to normal after a delay of several days. Campbell and Elliott[15] subsequently described two patients with long histories of paroxysmal tachycardia who, after the attacks ended, had T wave inversions that lasted 4 and 18 days. Cossio et al.[16] independently reported four patients with T wave abnormalities following paroxysmal tachycardia that resembled those seen after infarction; one patient who died had some cardiac dilatation but normal coronary vessels. In a follow-up report, Campbell[17] presented three additional cases of T wave abnormalities in patients whose histories "made it almost certain that the heart was normal except for the paroxysms," and Currie[18] described a 13-year-old girl with rapid paroxysmal tachycardia that terminated spontaneously after approximately 36 hours, and that was followed by T wave inversion in leads II and II, which did not return to normal until between 13 and 30 days after the attack.

Remarkable persistence of the posttachycardia T wave abnormalities was described in 1943 in a 38-year-old policeman who experienced a paroxysmal tachycardia at a rate of 230/min.[19] Quinidine, given over a few hours, terminated the tachycardia, but the T wave inversions in lead II did not return to normal until between 23 and 37 days later (Fig. 3). Ten years afterward, this patient experienced a second prolonged episode of tachycardia; quinidine was administered for only 2 days, but his T waves again did not become normal until between the 26th and 40th days after the episode of tachycardia.[19]

The introduction of electrical pacing provided further details as to the remarkable time course of the posttachycardia T wave syndrome. Chaterjee et al.[20] observed that long-lasting anterior T wave inversions could be induced after as little as 10 minutes of right ventricular pacing at a rate of 120/min, and that the extent of the abnormalities

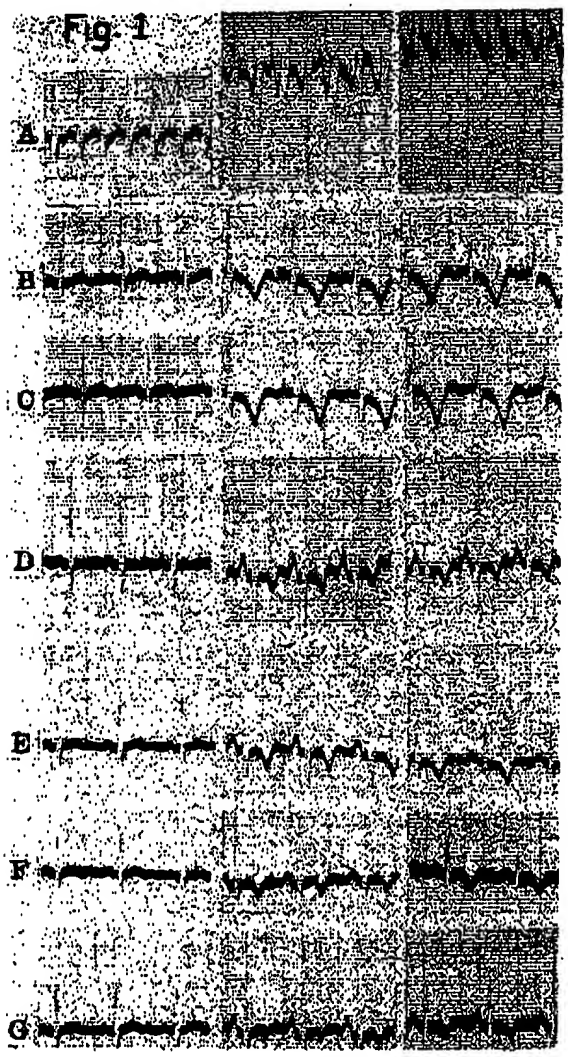

Figure 3. *Bipolar limb lead electrocardiograms during (A), and 1 (B), 2 (C), 4 (D), 16 (E), 23 (F), and 37 (G) days after an episode of tachycardia. The patient was given quinidine only during the first day, when the initial electrocardiogram had been obtained. (Reproduced with permission from Mosby-Year Book, Inc.[19])*